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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/526,323	10/03/2005	Richard H Ebright	744-47 PCT/US	6511

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EXAMINER	
KHANNA, HEMANT	
ART UNIT	PAPER NUMBER
1654	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/08/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

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Office Action Summary	Application No.	Applicant(s)	
	10/526,323	EBRIGHT, RICHARD H	
	Examiner	Art Unit	
	Hemant Khanna	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 December 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *78-120* is/are pending in the application.

4a) Of the above claim(s) *78-83 and 104-120* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *84-103* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *07/07/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election with traverse of claims 84-103 that belong to Group II in the reply filed on December 04, 2006 is acknowledged. The traversal is on the ground(s) that the Glinskii reference does not teach or disclose the claimed element "An analog of bacteriocidal peptide Microcin J25" (Response, third paragraph, page 03). Further, the Applicants argue that the species election be withdrawn because the Applicant's specification discloses the basis for linking RNAP from different species to form a common inventive concept (Response, first paragraph, page 04).

The applicant's arguments are not found persuasive. The expression "special technical feature" refers to those features that define a contribution which each of the claimed inventions, considered as a whole makes over the prior art. Thus, a feature found in the prior art cannot be considered to be a special technical feature. To the extent that the Applicant defines a peptide analog of microcin in claim 78 as one that differs from microcin J25 by atleast one amino acid substitution, insertion, or deletion, the peptides disclosed in the Glinskii reference meet the claimed limitations and by virtue of doing so, meet the requirements of the "special technical feature". Further Glinskii discloses methods (phage display and ELISA, page 26 and 27) to determine that the above-mentioned peptides bind the β' subunit of RNA polymerase and disrupt protein-protein contact regions in the subunit-subunit interactions during RNAP assembly (page 8, line 15). The Applicant is reminded that Claim 78 recites the activity of microcin analogs (functional property) with a potency at least equal to that of microcin J25, which is not given patentable weight.

MPEP 2112 reads "The claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable". Something which is old does not become patentable upon the discovery of a new property, use, or application. Even if the Applicant has discovered a new property (potency equal to that of MccJ25), such a discovery does not render the peptide analog itself new in the art. As such, since the scope of the peptides encompassed by Groups I, II and III includes the peptide sequences disclosed in the Glinskii reference, they cannot be considered a special technical feature.

The restriction between Groups I, II and III is maintained.

The requirement is still deemed proper and is therefore made FINAL.

With respect to the species election, the Applicant's arguments are not found persuasive in view of the Examiner's arguments above, and further in view of the arguments made in the Restriction requirement filed on October 06, 2006. Hence, the species requirement is maintained. The Applicant elected the species of intact bacterial RNAP, Escherichia coli, and RNA synthesis. The Applicant's species have not been found free of the art, and stand rejected under 35 USC 103(a) as set forth below.

Claims 78-120 are pending. Claims 78-83, and 104-120 are withdrawn from consideration as being drawn to a non-elected invention. Election was made **with** traverse in the reply filed on December 04, 2006.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 84-103 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, claims 84-103 are directed to identifying an agent that binds to RNAP secondary channel and derivatives of RNAP secondary channel having at least one substitution, insertion or deletion. Further, the claims are drawn to methods of identifying an agent that binds to a eukaryotic RNAP derivative when compared with an agent that binds to a bacterial RNAP secondary channel. While the specification has adequate written description of the RNAP secondary channel, there is no disclosure on the structural limitations of the genus represented by the derivatives of RNAP secondary channel and the genus represented by eukaryotic RNAP. Further, there is no disclosure of the activity of the

above-mentioned derivatives, nor any method to analyze the activity of the derivatives. There is no description of the identifying characteristics for recognizing that an agent will inhibit the activity of the derivative RNAP. One skilled in the art would conclude that the disclosure of intact RNAP secondary channel or eukaryotic RNAP is not representative of the undefined genus of derivatives recited in the claims. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus. Therefore, the inventor, at the time the application was filed was not in possession of the broad genus comprising "derivatives of bacterial RNAP secondary channel " and "derivatives of eukaryotic RNAP" needed to practice the claimed invention.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 84-103 rejected under 35 U.S.C. 103(a) as being unpatentable over Delgado et al (Journal of Bacteriology (2001) Vol. 183, pages 4543-4550) in view of Korzheva et al. (Science (2000) Vol. 289, pages 619-625), Darst et al (US 2002/0034808) and Woychik (Cell (February 2002) Vol. 108, pages 453-463).

The instant claims are drawn to methods of identifying an agent that inhibits RNA synthesis activity of E. coli RNA polymerase by binding to an RNAP secondary channel amino acid sequence. The claims further comprise comparing the inhibition by an agent that binds to the secondary channel with inhibition by an agent that binds to a mutant channel or one that binds to a eukaryotic RNAP.

With respect to claims 84-89, and 93-100, Delgado et al disclose methods to identify an agent that binds to the secondary channel by determining the binding site of the antibiotic MccJ25 within the intact E. coli RNA polymerase. Delgado further disclose that such methods involve contacting the RNA polymerase with the antibiotic and detecting the inhibition of RNA synthesis in presence of MccJ25 via a transcription assay (kinetics of binding, Materials and Methods). Delgado et al also disclose a mutant residing in the homology block G of the β' subunit (abstract) of RNA polymerase and comparative methods employing such a mutant in presence of the antibiotic versus the intact polymerase in presence of the antibiotic to identify the presence or absence of binding. Resistance to the antibiotic was indicative of the antibiotics ability to bind to RNA polymerase in the absence of the mutation. Delgado et al also disclose that the affected mutation is conserved in all prokaryotic homologues examined (Figure 2), which is good evidence to indicate that the region that contains the mutation is part of the catalytic center of the enzyme, and that which is responsible for the transcription properties of RNAP.

With respect to claims 84-89, and 93-100, Delgado differs from the instant claims by not explicitly reciting binding of the agent to the RNAP secondary channel.

With respect to claims 84-89, and 93-100, Korzheva disclose a model based on a bacterial x-ray crystal structure (page 620, first paragraph) known in the art wherein the secondary channel is responsible for the diffusion of incoming nucleotide substrates into the active site (Figure 3), to overcome access to the main channel which is blocked by the nucleic acid framework.

In view of the above teachings, it would have been obvious to one of ordinary skill in the art to use the method of identifying an agent that binds to a specific domain of RNAP to inhibit RNA synthesis, and to combine the method with agents with potential to bind to the secondary channel as modeled by Korzheva for the known and expected result of providing a means recognized in the art to identify regions in RNAP that contribute to sensitivity towards agents with inhibition of RNA synthesis activity for the development of a new antibiotic.

With respect to claims 90-92, and 101-103, Delgado disclose as discussed above. Further, Delgado disclose that the same comparative methods to detect activity in mutant bacterial RNAP can be applied to eukaryotes. The use of these methods resulted in locating the position of the mutant in Yeast (eukaryote). This mutant as disclosed corresponds exactly to the above-mentioned mutant in bacterial RNAP that confers resistance to the antibiotic MccJ25.

With respect to claims 90-92, and 101-103, Delgado et al differs from the instant claims by not explicitly reciting a derivative of human RNA polymerase.

With respect to claims 90-92, and 101-103, Darst et al disclose methods of identifying an agent for use as inhibitors of eukaryotic RNA polymerase (claim 11). Further, Darst et al disclose that that not all residues in the β' subunit of prokaryotic RNAP are conserved in eukaryotic RNA, pointing to the variable roles of the residues with respect to assembly and/or catalysis within the same subunit (paragraph 0179, 0176).

With respect to claims 90-91, and 101-102, Woychik et al disclose that human and yeast RNAP II share a much higher level of sequence identity at both the surface and core positions (page 457, paragraph 3). However, there is no significant conservation of surface residues between yeast RNAP II and bacterial RNAP (page 457, paragraph 4).

In view of the above teachings, it would have been obvious to one of ordinary skill in the art at the time of the invention to use the method of identifying an agent that binds to a specific domain of prokaryotic RNAP with eukaryotic RNAP (human or yeast) for the known and expected result of providing a means recognized in the art to identify the basis of differential specificity within species and how that specificity contributes to sensitivity towards agents capable of inhibiting RNA synthesis activity.

With respect to claims 92, and 103, in view of the above teachings, it would have been obvious to one of ordinary skill in the art at the time of the invention to use the method of identifying an agent that binds to the bacterial RNAP secondary channel wherein agents other than MccJ25 are tested against MccJ25 as a control for the known and expected result of providing a means recognized in the art to compare the binding

and inhibition properties of agents against a reference antibiotic known in the art to inhibit RNA synthesis by binding to RNAP.

Conclusion

6. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hemant Khanna whose telephone number is (571) 272-9045. The examiner can normally be reached on Monday through Friday, 7:30 am-4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Hemant Khanna Ph.D.
February 28, 2007

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